

University of Groningen

Biotine. Een bio-organische diskussie

Visser, Cornelis Maria

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

1977

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Visser, C. M. (1977). Biotine. Een bio-organische diskussie. s.n.

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

SUMMARY

This thesis begins with some introductory remarks on bioorganic chemistry in general and model studies of enzymatic reactions in particular (chapter I).

Thereafter a review is given of the chemistry and biochemistry of the prosthetic group biotin, a cofactor required for carboxyl transfer reactions in the metabolism (chapter II).

Biochemists traditionally describe biotin as a transferring agent, which carries "active carbon dioxide" between several substrates. This general type of function is shared by the other coenzymes. However, from the standpoint of organic chemistry, the carboxylated intermediate (1'-N-carboxybiotin) must be classified as an allophanate ion. These compound types are stable salts and miss the chemical reactivity expected of an activated intermediate. Moreover the biochemical proof that 1'-N-carboxybiotin is truly an intermediate could not be delivered despite repeated attempts.

To meet these problems the more reactive O-carboxybiotin was proposed as the true reactive intermediate and this on isolation isomerizes to 1'-N-carboxybiotin (or a derivative thereof) by way of an 1,3-O,N acyl migration, well known in organic chemistry.

Our attempts to make models for this O-carboxybiotin mediated reaction failed, presumably because of the facility of the acyl migration mentioned above (chapter III).

These attempts were stopped when renewed biochemical research demonstrated that 1'-N-carboxybiotin indeed is the only and true intermediate (chapter IV).

This means that the concept of biotin as a nucleophilic catalyst that lowers the transition state energy of the overall reaction is no longer tenable.

In our opinion the biotin mediated carboxylations can only be modeled if one activates both the biotin model and the counterpart of the acceptor molecule to the high energy enol forms (chapter V).

One can only speculate as to why during the origin of the metabolism this "detour" was selected. (chapter VI).